

7/8 The method of claim 1 wherein said promoter has a genotype selected from the group consisting of [TA]<sub>5</sub> / [TA]<sub>5</sub>, [TA]<sub>5</sub> / [TA]<sub>6</sub>, [TA]<sub>5</sub> / [TA]<sub>7</sub>, [TA]<sub>5</sub> / [TA]<sub>8</sub>, [TA]<sub>6</sub> / [TA]<sub>8</sub>, [TA]<sub>7</sub> / [TA]<sub>8</sub> and [TA]<sub>8</sub> / [TA]<sub>8</sub>.

5 10/12/13 9. A method for detecting polymorphisms in the uridine diphosphate glucuronosyltransferase I (UGT1A1) gene promoter comprising determining the number of thymidine-adenine, (TA) repeats in said promoter, wherein the number of TA repeats correlates with expression of the gene.

10 9/10 The method of claim 9 comprising the steps of:  
(a) obtaining DNA from an individual;  
(b) amplifying all or part of said UGT gene promoter contained in said DNA; and  
(c) determining the number of TA repeats in said promoter.

15 10/11 The method of claim 9 wherein said DNA being amplified comprises all or part of a UGT1A1 promoter.

20 11/12 The method of claim 9 wherein said DNA is amplified by polymerase chain reaction (PCR) and said number of TA repeats is determined by gel electrophoresis.

25 12/13 The method of claim 9 wherein said DNA is amplified by PCR and said number of TA repeats is determined by sequencing said amplified DNA.

30 14. The method of claim 9 wherein said polymorphism comprises an allele, said allele selected from the group consisting of five TA repeats, [TA]<sub>5</sub>, six TA repeats, [TA]<sub>6</sub>, seven TA repeats, [TA]<sub>7</sub> and eight TA repeats, [TA]<sub>8</sub>.

13 15. The method of claim 8 wherein said promoter has a genotype selected from the group consisting of [TA]<sub>5</sub> / [TA]<sub>5</sub>, [TA]<sub>5</sub> / [TA]<sub>6</sub>, [TA]<sub>5</sub> / [TA]<sub>7</sub>, [TA]<sub>5</sub> / [TA]<sub>8</sub>, [TA]<sub>6</sub> / [TA]<sub>8</sub>, [TA]<sub>7</sub> / [TA]<sub>8</sub> and [TA]<sub>8</sub> / [TA]<sub>8</sub>.

5 13 16. A method for screening individuals for variation in glucuronidation activity comprising detecting polymorphisms in a uridine diphosphate glucuronosyltransferase (UGT) gene promoter comprising determining the number of thymidine-adenine (TA) repeats in said promoter, wherein the number of TA repeats correlates with expression of the gene.

10 15 17. The method of claim 16 comprising the steps of:  
(a) obtaining DNA from an individual;  
(b) amplifying all or part of said UGT gene promoter contained in said DNA; and  
15 (c) determining the number of TA repeats in said promoter.

16 18. The method of claim 14 or 15 wherein said promoter is the UGT1A1 promoter.

20 17 19. The method of claim 18 wherein said DNA being amplified comprises all or part of a UGT1A1 promoter.

25 18 20. The method of claim 14 wherein said DNA is amplified by the polymerase chain reaction (PCR) and said number of TA repeats is determined by gel electrophoresis.

30 19 21. The method of claim 14 wherein said DNA is amplified by PCR and said number of TA repeats is determined by sequencing said amplified DNA.

22. The method of claim 16 wherein said polymorphism comprises an allele, said allele selected from the group consisting of five TA repeats, [TA]<sub>5</sub>, six TA repeats, [TA]<sub>6</sub>, seven TA repeats, [TA]<sub>7</sub>, and eight TA repeats, [TA]<sub>8</sub>.

23. The method of claim 16 wherein said promoter has a genotype selected from the group consisting of [TA]<sub>5</sub> / [TA]<sub>5</sub>, [TA]<sub>5</sub> / [TA]<sub>6</sub>, [TA]<sub>5</sub> / [TA]<sub>7</sub>, [TA]<sub>5</sub> / [TA]<sub>8</sub>, [TA]<sub>6</sub> / [TA]<sub>8</sub>, [TA]<sub>7</sub> / [TA]<sub>8</sub> and [TA]<sub>8</sub> / [TA]<sub>8</sub>.

24. A method for screening individuals for variation in glucuronidation activity comprising detecting polymorphisms in a uridine diphosphate glucuronosyltransferase 1 (UGT1A1) gene promoter, the method comprising determining the number of thymidine-adenine (TA) repeats in said promoter, wherein the number of TA repeats in said promoter correlates with expression of the UGT gene.

25. The method of claim 24 comprising the steps of:

- (a) obtaining DNA from an individual;
- (b) amplifying all or part of said UGT gene promoter contained in said DNA; and
- (c) determining the number of TA repeats in said promoter;

26. The method of claim 24 wherein said DNA being amplified comprises all or part of a UGT1A1 promoter.

27. The method of claim 24 wherein said DNA is amplified by polymerase chain reaction (PCR) and said number of TA repeats is determined by gel electrophoresis.

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28. The method of claim 24 wherein said DNA is amplified by PCR and said number of TA repeats is determined by sequencing said amplified DNA.

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5 29. The method of claim 24 wherein said polymorphism comprises an allele, said allele selected from the group consisting of five TA repeats, [TA]<sub>5</sub>, six TA repeats, [TA]<sub>6</sub>, seven TA repeats, [TA]<sub>7</sub> and eight TA repeats, [TA]<sub>8</sub>.

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30. The method of claim 24 wherein said promoter has a genotype selected from the group consisting of [TA]<sub>5</sub> / [TA]<sub>5</sub>, [TA]<sub>5</sub> / [TA]<sub>6</sub>, [TA]<sub>5</sub> / [TA]<sub>7</sub>, [TA]<sub>5</sub> / [TA]<sub>8</sub>, [TA]<sub>6</sub> / [TA]<sub>8</sub>, [TA]<sub>7</sub> / [TA]<sub>8</sub> and [TA]<sub>8</sub> / [TA]<sub>8</sub>.

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31. A method for optimizing drug dosages for a patient wherein said drugs are glucuronidated by a uridine diphosphate glucuronosyltransferase (UGT), said method comprising determining the number of thymidine-adenine (TA) repeats in a promoter of the UGT gene wherein the number of TA repeats correlates with expression of said UGT gene, and wherein the activity of said drug is effected by its level of glucuronidation.

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32. The method of claim 31 comprising the steps of:  
(a) obtaining DNA from an individual;  
(b) amplifying all or part of said UGT gene promoter contained in said DNA; and  
25 (c) determining the number of TA repeats in said promoter.

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33. The method of claim 31 or 32 wherein said promoter is the UGT1A1 promoter.

*C*  
*cont'd*  
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34. The method of claim 32 wherein said DNA being amplified comprises all or part of a UGT1A1 promoter.

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35. The method of claim 31 wherein said DNA is amplified by the polymerase chain reaction (PCR) and said number of TA repeats is determined by gel electrophoresis.

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36. The method of claim 31 wherein said DNA is amplified by PCR and said number of TA repeats is determined and sequencing said amplified DNA.

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37. The method of claim 31 wherein said polymorphism comprises an allele, said allele selected from the group consisting of five TA repeats, [TA]<sub>5</sub>, six TA repeats, [TA]<sub>6</sub>, seven TA repeats, [TA]<sub>7</sub>, and eight TA repeats, [TA]<sub>8</sub>.

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38. The method of claim 31 wherein said promoter has a genotype selected from the group consisting of [TA]<sub>5</sub> / [TA]<sub>5</sub>, [TA]<sub>5</sub> / [TA]<sub>6</sub>, [TA]<sub>5</sub> / [TA]<sub>7</sub>, [TA]<sub>5</sub> / [TA]<sub>8</sub>, [TA]<sub>6</sub> / [TA]<sub>8</sub>, [TA]<sub>7</sub> / [TA]<sub>8</sub> and [TA]<sub>8</sub> / [TA]<sub>8</sub>.

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39. A method for optimizing drug dosages wherein said drugs are glucuronidated by uridine diphosphate glucuronosyltransferase I, said method comprising determining the number of thymidine-adenine (TA) repeats in a promoter of the UGT1 gene wherein the number of TA repeats correlates with expression of said UGT gene, and wherein the activity of said drug is effected by its level of glucuronidation.

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40. The method of claim 39 comprising the steps of:  
(a) obtaining DNA from an individual;

(b) amplifying all or part of said UGT gene promoter contained in said DNA; and

(c) determining the number of TA repeats in said promoter.

5 <sup>37</sup><sub>41.</sub> The method of claim <sup>35</sup><sub>39</sub> or <sup>36</sup><sub>40</sub> wherein said promoter is the UGT1A1 promoter.

<sup>38</sup><sub>42.</sub> The method of claim <sup>35</sup><sub>39</sub> wherein said DNA being amplified comprises all or part of a UGT1A1 promoter.

10 <sup>39</sup><sub>43.</sub> The method of claim <sup>35</sup><sub>39</sub> wherein said DNA is amplified by the polymerase chain reaction (PCR) and said number of TA repeats is determined by gel electrophoresis.

15 <sup>40</sup><sub>44.</sub> The method of claim <sup>35</sup><sub>39</sub> wherein said DNA is amplified by PCR and said number of TA repeats is determined by sequencing said amplified DNA.

20 <sup>41</sup><sub>45.</sub> The method of claim <sup>35</sup><sub>39</sub> wherein said polymorphism comprises an allele, said allele selected from the group consisting of five TA repeats, [TA]<sub>5</sub>, six TA repeats, [TA]<sub>6</sub>, seven TA repeats, [TA]<sub>7</sub>, and eight TA repeats, [TA]<sub>8</sub>.

25 <sup>42</sup><sub>46.</sub> The method of claim <sup>35</sup><sub>39</sub> wherein said promoter has a genotype selected from the group consisting of [TA]<sub>5</sub> / [TA]<sub>5</sub>, [TA]<sub>5</sub> / [TA]<sub>6</sub>, [TA]<sub>5</sub> / [TA]<sub>7</sub>, [TA]<sub>5</sub> / [TA]<sub>8</sub>, [TA]<sub>6</sub> / [TA]<sub>8</sub>, [TA]<sub>7</sub> / [TA]<sub>8</sub> and [TA]<sub>8</sub> / [TA]<sub>8</sub>.

30 <sup>43</sup><sub>47.</sub> A method for predicting an individual's sensitivity to xenobiotics wherein said xenobiotics are glucuronidated by a uridine diphosphate glucuronosyltransferase gene product, said method comprising determining the

number of thymidine-adenine (TA) repeats in a UGT gene promoter, wherein the number of TA repeats correlates with expression of said UGT gene and wherein the individual's sensitivity to said xenobiotics is effected by glucuronidation activity.

- 44/48. The method of claim 43 comprising the steps of:
- (a) obtaining DNA from an individual;
  - (b) amplifying all or part of said UGT gene promoter contained in said DNA; and
  - (c) determining the number of TA repeats in said promoter.

10 45/49. The method of claim 43 or 44 wherein said promoter is the UGT1A1 promoter.

15 46/50. The method of claim 43 wherein said DNA being amplified comprises all or part of a UGT1A1 promoter.

47/51. The method of claim 43 wherein said DNA is amplified by the polymerase chain reaction (PCR) and said number of TA repeats is determined by gel electrophoresis.

20 48/52. The method of claim 43 wherein said DNA is amplified by PCR and said number of TA repeats is determined by sequencing said amplified DNA.

25 49/53. The method of claim 43 wherein said polymorphism comprises an allele, said allele selected from the group consisting of five TA repeats, [TA]<sub>5</sub>, six TA repeats, [TA]<sub>6</sub>, seven TA repeats, [TA]<sub>7</sub>, and eight TA repeats, [TA]<sub>8</sub>.

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54. The method of claim 47 wherein said promoter has a genotype selected from the group consisting of [TA]<sub>5</sub> / [TA]<sub>5</sub>, [TA]<sub>5</sub> / [TA]<sub>6</sub>, [TA]<sub>5</sub> / [TA]<sub>7</sub>, [TA]<sub>5</sub> / [TA]<sub>8</sub>, [TA]<sub>6</sub> / [TA]<sub>8</sub>, [TA]<sub>7</sub> / [TA]<sub>8</sub> and [TA]<sub>8</sub> / [TA]<sub>8</sub>.

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55. A method for predicting an individual's sensitivity to xenobiotics wherein said xenobiotics are glucuronidated by a uridine diphosphate glucuronosyltransferase I gene product, said method comprising determining the number of thymidine-adenine (TA) repeats in a UGT1 gene promoter, wherein the number of TA repeats correlates with expression of said UGT1 gene and wherein  
10 the individual's sensitivity to said xenobiotics is effected by glucuronidation activity.

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56. The method of claim 55 comprising the steps of:  
(a) obtaining DNA from an individual;  
(b) amplifying all or part of said UGT1 gene promoter contained  
15 in said DNA; and  
(c) determining the number of TA repeats in said promoter.

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57. The method of claim 55 or 56 wherein said promoter is the UGT1A1 promoter.

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58. The method of claim 55 wherein said DNA being amplified comprises all or part of a UGT1A1 promoter.

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59. The method of claim 55 wherein said DNA is amplified by the polymerase chain reaction (PCR) and said number of TA repeats is determined  
25 by gel electrophoresis.

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60. The method of claim 55 wherein said DNA is amplified by PCR and said number of TA repeats is determined by sequencing said amplified  
30 DNA.



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61. The method of claim 55 wherein said polymorphism comprises an allele, said allele selected from the group consisting of five TA repeats, [TA]<sub>5</sub>, six TA repeats, [TA]<sub>6</sub>, seven TA repeats, [TA]<sub>7</sub>, and ~~eight TA repeats, [TA]<sub>8</sub>.~~

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62. The method of claim 55 wherein said promoter has a genotype selected from the group consisting of [TA]<sub>5</sub> / [TA]<sub>5</sub>, [TA]<sub>5</sub> / [TA]<sub>6</sub>, [TA]<sub>5</sub> / [TA]<sub>7</sub>, [TA]<sub>5</sub> / [TA]<sub>8</sub>, [TA]<sub>6</sub> / [TA]<sub>8</sub>, [TA]<sub>7</sub> / [TA]<sub>8</sub> and [TA]<sub>8</sub> / [TA]<sub>8</sub>.

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63. A kit for detecting polymorphisms in a uridine diphosphate glucuronosyltransferase (UGT) gene promoter wherein the number of thymidine-adenine (TA) repeats in said UGT gene promoter correlates to expression of said UGT gene, the kit comprising primers for amplifying DNA comprising all or part of the UGT gene promoter to determine the number of TA repeats in said promoter.

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64. The kit of claim 63 wherein said kit contains one or more additional components selected from the group consisting of deoxynucleoside triphosphates, buffers, labels for detecting said polymorphisms and instructions.

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65. The kit of claim 63 or 64 wherein the primers are selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 and SEQ ID NO: 4.

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66. The kit of claim 63 or 64 wherein said promoter is the UGT1A1 promoter.

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67. A kit for detecting polymorphisms in a uridine diphosphate glucuronosyltransferase I (UGT1A1) gene promoter wherein the number of thymidine-adenine (TA) repeats in said UGT1 gene promoter correlates to

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expression of said UGT1 gene, the kit comprising primers for amplifying DNA comprising all or part of the UGT1 gene promoter to determine the number of TA repeats in said promoter.

5                    68.     The kit of claim 67 wherein said kit contains one or more additional components selected from the group consisting of deoxynucleoside triphosphates, buffers, labels for detecting said polymorphisms and instructions.

10                   69.     The kit of claim 67 or 68 wherein the primers are selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 and SEQ ID NO: 4.

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